Remarks

Claims 22-42 are currently pending in this application.

The Office Action objected to the specification as having an improper format and required a substitute specification; objected to the title of the invention as not being descriptive; and rejected claims 1-21 35 U.S.C. § 102(b) as being anticipated by Foo et al. (U.S. Patent No. 5,604,435).

Applicants have submitted a substitute specification and a new title that address the objections noted by the Office Action. Therefore, Applicants respectfully request reconsideration and withdrawal of the objections to the specification and title.

Newly submitted claims 22-42 mirror originally-filed claims 1-21. Thus, it is necessary to address the prior art rejection of claims 1-21 even though this rejection is moot in light of the cancellation of claims 1-21. Applicants respectfully traverse the prior art rejection of claims 1-21, for the following reasons.

Foo et al. disclose separating the data acquired from a first echo time TE_1 and a second distinct echo time TE_2 into data blocks 100 and 111. (Col. 6, lines 61-67). That is, Foo et al. disclose using two separate and distinct echo times (TE_1, TE_2) during the data acquisition period, and then separating the data acquired from these two separate and distinct echo times. However, Foo et al. fail to disclose separating data from a single echo time into two parts that are differently dependent upon the single echo time.

The present invention recited, for example, in claim 22-24, comprises a combination of elements, including at least one analyzing means that separates the data into at least two parts that are differently dependent on an echo time T_E. Similarly, the present invention recited in claim 25, and claims 26-42, at least by virtue of dependence, comprises a combination of elements, including

separating the data into at least two parts that are differently dependent on an echo time T_E. Thus, in the present invention, the NMR data is separated into two parts that differently depend upon a single echo time T_E.

In contrast, Foo et al. fail to disclose the combination of elements recited in claims 22-42. Specifically, Foo et al. fail to disclose separating NMR data into two parts that differently depend upon a single echo time T_E. Rather, the reference discloses using two separate and distinct echo times (TE_1, TE_2) during the data acquisition period, and then separating the data acquired from these two separate and distinct echo times. In Foo et al., data is not separated from a single echo time, but rather from two separate and distinct echo times. Since the reference fails to disclose separation of data from a single echo time, it cannot possibly disclose separation of data into parts that differently depend upon a single echo time, as recited in claims 22-42.

In addition to the above, Applicants believe that Foo et al. fail to disclose many of the features of dependent claims 23 and 26-42. For example, Foo et al. fail to disclose the very specific steps recited in claims 41 and 42.

In light of the above, Applicants submit that claims 22-42 are patentably distinguishable from Foo et al. Applicants, therefore, respectfully request reconsideration and withdrawal of the Section 102(b) rejection of claims 1-21.

In view of the foregoing remarks, Applicants submit that the claimed invention, as amended, is neither anticipated nor rendered obvious in view of the prior art references cited against this application. Applicants therefore request the reconsideration of the application and the timely allowance of the pending claims.

If there are any other fees due in connection with the filing of this response, please charge the

fees to our Deposit Account No. 03-2775. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

CONNOLLY BOVE LODGE & HUTZ LLP

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BACKGROUND OF THE INVENTION

A. Field of the Invention

The present invention ~~pertains~~ relates generally to a computer-implemented system and method for analyzing data from ~~measurements of~~ nuclear magnetic resonance measurements, whereby the data contains at least one relaxation signal of a sample. More particularly, the present

~~The~~ invention ~~also~~ relates to a nuclear magnetic resonance tomograph and to a method for analyzing data from ~~measurements of~~ nuclear magnetic resonance measurements wherein~~, a process in which~~ at least one relaxation signal of a sample is determined.

B. Description of the Related Art

Nuclear magnetic resonance (NMR) is ~~employed in order~~used to obtain a contrast image of an object or spectroscopic information about a substance. Magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) make it possible to examine regional hemodynamics *in vivo* with changes in blood volumes and blood states, as well as changes in the metabolism as a function of brain activity.~~;~~ See S. Posse *et al.*, Functional Magnetic Resonance Studies of Brain Activation; Seminars in Clinical Neuropsychiatry, Vol. 1, No. 1., pp. 76-88 (1996)~~, pages 76 through 88~~.

~~Particularly in~~In medical research~~,~~ there is a need to acquire information about brain activity by means of measurements of blood flow or changes in the concentration of deoxyhemoglobin (DOH). Neuronal activation is ~~manifested~~ shown by an increase of the blood flow into activated regions of the brain, whereby a drop occurs in the concentration of ~~deoxyhemoglobin~~DOH. ~~Deoxyhemoglobin (~~DOH~~)~~ is a paramagnetic substance that reduces the magnetic field homogeneity and thus accelerates the signal relaxation. If the DOH concentration

drops due to brain activity that triggers blood flow, then the signal relaxation in the active regions of the brain is modulated. It is primarily due to the excitation of the protons of hydrogen protons in water that are excited. A localization of brain Brain activity localization is made possible by conducting an examination with functional NMR methods that measure the NMR signal with a time delay (i.e., echo time). This is also referred to as a susceptibility-sensitive measurement. The biological mechanism of action is known in the literature underas the name BOLD effect (Blood Oxygenation Level Dependence) effect). and, in In susceptibility-sensitive magnetic resonance measurements at a field strength of a static magnetic field of, for example, 1.5 teslaTesla, it the BOLD effect leads to fluctuations of the image brightness of up to 10% in activated regions of the brain. Instead ofBesides the endogenous contrast agent DOH, other contrast agents can also occur that cause a change in the susceptibility. NMR imaging methods select slices or volumes that yield a measurement signal under appropriate irradiation with high-frequency pulses and under the application of magnetic gradient fields.; this This measurement signal is digitized and stored in a two-dimensional or three-dimensional field in the measuringa computer.

A two-dimensional or three-dimensional Fourier transform on the basis ofbased upon the raw data collected then serves to acquire (reconstructs) the desired image information.

A reconstructed slice image consists of pixels (picture elements), and a volume data set consists of voxels (volume elements). A pixel is a two-dimensional picture element, for instance, that may be in the shape of, for example, a square. The image is made up of the pixels. A voxel is a three-dimensional volume element that may be in the shape of, for example, a cube which, for metrological reasons, does not exhibit any sharp boundaries. The dimensions of a pixel normally lie in the order of magnitude ofare typically about 1 mm^2, and those the dimensions of

a voxel ~~in the order of magnitude of~~are typically about 1 mm^3. The geometries and dimensions ~~can~~ of pixels and voxels, however, may vary.

Since experiments have shown that it is never possible to assume a strictly two-dimensional plane in the case of slice images, the term voxel is often employed ~~here as well since this~~because it takes into consideration the fact that the image planes extend into the third dimension.

By comparing the measured signal course in every pixel with the time course of a model function, a stimulus-specific neuronal activation can be detected and spatially localized. A stimulus can be, for ~~instance~~example, a somatosensorial, acoustic, visual or olfactory stimulus as well as a mental or motor task. The model function or the model time series describes the anticipated signal change of the magnetic resonance signal resulting from neuronal activation. These can be derived, for example, by means of empirical rules from a paradigm of the experiment in question. The essential aspect is to ~~take into consideration~~consider a time delay of the model function with respect to the paradigm (i.e., sluggish reaction of the blood flow in response to neuronal activation).

~~It is already known how~~Depiction of brain activation ~~can be depicted~~ by activation images acquired from nuclear spin tomographic data has been performed. The activation images can ~~even~~ be computed and displayed in real time, that is ~~to say~~, a data set can be converted into an image before the next data set is measured. ~~Here~~, wherein the time interval is typically 1 to 3 seconds.

~~Such a c~~Computation and reproduction of ~~the~~ activation images in real time are described in U.S. ~~patent~~ Patent ~~no~~No. 5,657,755. ~~This method is characterized by the fact that it allows a,~~ wherein the activation images have a high resolution~~, both~~ in ~~terms of~~ time and space.

Another ~~known~~conventional activation images method is ~~presented~~ disclosed in the articles by P. Jezzard~~, P.~~ *et al.*, Proc. SMRM, p. 1392 (-1993)~~, page 1392~~; B. Biswal~~. B.~~ *et al.*, MRM 34, p. 537 (1995)~~ page 537~~; and P. Purdon~~, P.~~ *et al.*, Proc. ISMRM, p. 253 (1998)~~, page 253~~. This method ~~makes use of~~uses a measuring signal and a paradigm of the measurement~~.~~ ~~Both~~, wherein both signals undergo a Fourier transform.

All of the above-mentioned ~~The known~~ conventional methods analyze the similarity between the ~~signal of the~~ paradigm signal and ~~of~~ the measured data signal. Thus, there is a need in the art for a method for analyzing NMR data that overcomes the deficiencies of the related art.

~~The invention has the objective of carrying out a method of the known type in such a way that the highest possible contrast-to-noise ratio is achieved.~~

SUMMARY OF THE INVENTION

The present invention solves the problems of the related art by providing ~~According to the invention, this objective is achieved in that~~ a computer-implemented system and method that ~~of the known type is configured in such a way that the computer operates with at least one analyzing means, whereby said analyzing means~~ separates ~~the~~ NMR data into at least two parts that are differently dependent on an echo time T_E.

In accordance with the purpose of the invention, as embodied and broadly described herein~~In particular~~, the present invention ~~provides~~includes ~~for~~ a computer-implemented system that performs ~~with which~~ a fast spectroscopic imaging method ~~can be realized~~ that detects the changes in the NMR signal relaxation using a time constant $T_2^* = \frac{1}{R_2^*}$ at several points in time following excitation.

~~This~~ The spectroscopic imaging method of the present invention is preferably an echo-planar imaging method, and more preferably ~~especially~~ a repeated, two-dimensional echo-imaging method ~~consisting of a~~that repeatedly uses ~~of~~ two-dimensional echo-planar image encoding. Spatial encoding takes place within the shortest possible time span that is repeated several times during one signal decay and preferably ranges from 20 ms to 100 ms. The ~~multiple~~ repetition of the echo-planar encoding during one signal decay depicts the course of the signal decay in the sequence of reconstructed individual images.

~~A practical conventional~~An echo-planar method useful for the present invention is ~~designated as~~ EPI (Echo-Planar-Imaging), and, more preferably, ~~. An advantageous implementation of the method according to the invention is done by means of~~ TURBO-PEPSI (Proton Echo Planar Spectroscopic Imaging).

The number of images that are encoded during the signal decay is dependent upon the relaxation time and ~~on~~ the encoding time Δt for a single image.

Preferably, a computer is used to analyze data from nuclear magnetic resonance tomography, ~~a process in which~~wherein the data contains at least one relaxation signal of a sample. The computer-implemented method of the present invention separates ~~and in which~~ the data ~~is separated~~ into parts that are dependent on an echo time T_E and into at least one ~~more component~~part that is not dependent on the echo time T_{E_2} ~~and~~ whereby the signals that are dependent on an echo time T_E are acquired as activation signals. The computer may include an analyzing means (e.g., a microprocessor) that performs the method of the present invention.

~~A noise signal can be detected in that the computer operates with at least one analyzing means which separates the data into at least one part that is dependent on an echo time T_E and~~

~~into another component that is not dependent on the echo time T_E, whereby the analyzing means acquires signals that are dependent on an echo time T_E as activation signals.~~

~~A separation of s~~Several components of a function to be examined can be ascertained with the present invention by determining the signals that have a different dependence on the echo time T_E. Thus, it is possible~~, for instance,~~ with the present invention to separate an amplitude δ_0 from a time constant T_2^* and/or from a noise signal g.

Further in accordance with the purpose of the invention, as embodied and broadly described herein~~Moreover~~, the present invention relates to a nuclear magnetic resonance tomograph that ~~comprises~~ includes at least one computer performing the method of the present~~according to the~~ invention.

~~The invention also provides that a method to analyze data from nuclear magnetic resonance tomography whereby at least one relaxation signal of a sample is determined is carried out in such a way that the data is separated into at least two parts having a different dependence on an echo time T_E.~~

Preferably, the ~~process~~ method of the present invention ~~is to be carried out in such a way that~~acquires intensity values of the measured data for identical echo times ~~are acquired~~ in at least two different recordings of the relaxation signal and ~~in that~~subsequently acquires a dependence of the intensity values on the echo time T_E~~, is subsequently acquired and in that~~wherein the relaxation signal is separated into parts having a different dependence on the echo time T_E.

Preferably, the ~~method should be carried out in such a way that the~~ relaxation signal is divided into a part that is dependent on ~~an~~ the echo time T_E and into at least one part that is not dependent on the echo time T_E, wherein ~~and so that~~ the part that is dependent on the echo time T_E is acquired as an activation signal.

~~In this context, it~~It is especially advantageous for at least one detected signal to be ~~detected that is~~ proportional to $T_E \exp(-T_E / T_2^*)$, whereby the value of T_2^* is determined particularly by means of a preferably separate fit procedure on the basis of the same data.

~~Here, it is particularly practical for~~ T_2^* ~~to~~ may be calculated with the following formula:

$$S = S_0 \exp(-T_E / T_2^*) + g ,$$

~~Furthermore, it is advantageous to carry out the method in such a way that~~wherein the statistical fluctuations ΔT_2^* are determined. In a preferred embodiment of the present invention, the following calculations are performed by the computer-implemented method of the present invention:

~~In this context, it is especially practical for~~ a standard deviation $\sigma(\Delta T_2^*)$ ~~to be calculated.~~

~~It is likewise advantageous for~~ a quotient $\sigma(\Delta T_2^*) / T_2^*$ to be formed and acquired as a measure of an activity;

~~Here, it is particularly practical for~~ a statistical deviation of an initial intensity S_0 ~~to be determined.~~

~~Here, it is advantageous for~~ a standard deviation $\sigma(S_0)$ ~~to be calculated.~~

~~In this context, it is preferable for~~ a quotient $\sigma(S_0) / S_0$ ~~to be calculated.~~

~~Particular preference is given to carrying out the method in such a way that~~ a statistical fluctuation of a noise signal g; and ~~is determined.~~

~~Here, it is especially advantageous for~~ a standard deviation σ(g) ~~of g to be formed~~.

Moreover, the computer-implemented method of the present invention ~~is~~ preferably ~~carried out in such a way that~~acquires the recorded data ~~is acquired~~ in ~~an~~ at least a two-

dimensional field, whereby a field axis (DTE) acquires echo times T_E and whereby another field axis (DTR) reproduces repetitions of excitations at a time interval T_R.

~~Here, it~~It is particularly advantageous for $\sigma(\Delta T_2^*)$ and σ(g) to be determined by means of the following steps:

(i) adaptation of signals averaged over the other field axis (DTR) to an exponential decay as a function of the first field axis (DTE) and determination of S_0 and T_2^*;

(ii) calculation of $\sigma(\Delta S_0)$, $\sigma(\Delta T_2^*)$ and σ(g) for several voxels and different T_E, followed by averaging of these values over at least one region of interest (ROI);

(iii) adaptation of

$$\frac{\sigma(\Delta S)}{S_0} = \left\{\left[\left(\frac{T_E}{T_s^*}\right)^2\left(\frac{\sigma\left(\Delta T_2^*\right)}{T_2^*}\right)^2 + \left(\frac{\sigma\left(\Delta S_0\right)}{S_0}\right)^2 - 2\frac{T_E}{T_2^*}\frac{\left(\Delta S_0 \Delta T_2^*\right)}{S_0 T_2^*}\right] e^{-2T_E/T_2^*} + \left(\frac{\sigma(g)}{S_0}\right)^2\right\}$$; and

~~and~~ (iv) determination of σ(ΔS) / S_0 as a function of T_E.

~~Here, it~~It is also particularly advantageous for the expression $< \Delta S_0 \Delta T_2^* >= 0$ to be used for the adaptation of $\sigma(\Delta S_0)/S_0$.

~~Additional advantages, special features and practical refinements of the invention can be gleaned from the subordinate claims and from the following presentation of preferred embodiments of the invention with reference to model calculations, drawings and a table.~~

~~The drawings show the following:~~

Further scope of applicability of the present invention will become apparent from the detailed description given hereinafter. However, it should be understood that the detailed description and specific examples, while indicating preferred embodiments of the invention, are given by way of illustration only, since various changes and modifications within the spirit and

scope of the invention will become apparent to those skilled in the art from this detailed description. It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the invention, as claimed.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will become more fully understood from the detailed description given hereinbelow and the accompanying drawings which are given by way of illustration only, and thus are not limitative of the present invention, and wherein:

Figure 1 ——is a schematic diagram showing a multi-echo sequence with several measuring sequences, each of which follows a spin excitation (*) and ~~involving~~ involves the acquisition of various echo times T_E;

Figure 2 ——is a schematic diagram ~~that serves to illustrate~~showing a method involving the separate preparation of data for each of the echo times;

Figure 3 ——are graphs showing an experimental differential signal of a functional relaxation time change in a selected picture element as a function of the measuring time following a signal excitation;

Figure 4 ——are graphs showing ΔS from various voxels averaged over a few ROIs as a function of T_E for two representative persons; and

Figure 5 ——are actual images, wherein ~~in~~ the upper ~~portion of the~~ image~~, a~~ shows detection of brain activation in four steps ~~by means of~~using a conventional imaging method and~~,~~ ~~in~~ the lower ~~portion of the~~ image~~, a~~ shows detection of brain activation ~~by means of a~~using the method ~~according to~~of the present invention.

~~The table shows a compilation of the experimental sample data.~~

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The following detailed description of the invention refers to the accompanying drawings. The same reference numbers in different drawings identify the same or similar elements. Also, the following detailed description does not limit the invention. Instead, the scope of the invention is defined by the appended claims and equivalents thereof.

Figure 1 depicts a multi-echo sequence with several measuring sequences, each of which follows a spin excitation (*) and ~~involving~~ involves the acquisition of various echo times T_E.

The measuring sequences of the multi-echo sequence were determined by means of the ~~Turbo~~TURBO-PEPSI method. Each of the measuring sequences contains twelve echo signals with echo times that lie between 12 and 213 ms. The echo times were each acquired in the form of a time interval ΔT_E ~~lasting~~ of 18.3 ms.

The values ~~given for~~of the echo times and the time intervals are ~~each~~ adapted to the speed of the data processing. ~~Particularly in the case of a~~With further improvements in scanner technology, it will be possible to raise the number of echo signals and to shorten the time intervals ΔT_E.

Figure 2 ~~depicts~~ is a schematic diagram showing how differing measuring sequences are used to acquire a signal at a first echo time or at a second or subsequent echo time.

In the curve depicted in Figure 3, a measuring signal $\sigma(S)$ has been acquired as a function of the echo time. ~~It~~ Figure 3 further shows ~~a principle involving~~ a fit procedure that serves to divide the measuring signal $\sigma(S)$ into components that are dependent on T_2^* and into noise that is not dependent on T_E. The measuring signal $\sigma(S)$ consists of a part that is dependent on an

amplitude S_0, ~~and~~ of a part that is dependent on a relaxation time T_2^*, and of a constant noise signal g.

~~In particular, the~~The computer-implemented system and method of the present invention ~~provides for achieving a differentiation~~differentiates between activation signals and noise by ~~means of an analysis of~~ analyzing the course of time of the measured data and/or their statistical distribution.

The analysis method ~~according to~~of the present invention ~~can~~ may be checked experimentally~~, for example, by means of~~with, for example, nuclear spin tomographic examinations of the brains of test subjects. A source of light, ~~especially~~ preferably a matrix of light-emitting diodes (LED), ~~is~~ may be positioned directly in front of the face of the test subjects and then excited ~~so as~~ to emit flash signals. The frequency of excitation ~~is 8~~may be eight Hz. The effect of the signal flashes ~~is~~ may be exerted over a time interval — synchronized with the carrier signal from a scanner — of several seconds~~, for instance,~~ (e.g., five~~5~~ seconds), which is followed by a rest interval of approximately the same duration. The ~~scanner~~ source of light may be ~~is~~ a Vision 1.5 Tesla, full-body scanner made by Siemens Medical Systems of Erlangen, Germany, with a magnetic field gradient of 25 mT/m. Such a scanner is able to switch over gradient fields within about 600 µs.

TURBO-PEPSI (Proton Echo Planar Spectroscopic Imaging) ~~was~~ may be employed as the spectroscopic imaging method.

Data adaptation ~~was~~ may be performed according to the exponential function~~:~~

$S = S_0 e^{-T_E/T_2^*}$, and

making use of a non-linear least-square-fit.

~~A~~ The differentiation between activation and noise ~~by means of~~with multi-echo fMRI will ~~be presented below~~now be described.

The detection of physiological noise (caused, for example, by a heart beat) ~~calls for~~requires a stationary frequency spectrum~~,~~ for adequate temporal resolution ~~as well as for~~and prior knowledge about the spatial and temporal characteristics of the noise. ~~According to the~~The present invention~~,~~ provides a new method for differentiating between BOLD-related variations and other fluctuations of the MR signal (caused, for ~~instance~~example, by thermal noise) ~~is being proposed that can completely do~~ without any prior knowledge of a stimulation paradigm. ~~This~~ The method of the present invention is based upon a single-shot-multi-echo sequence ~~like~~similar to the ~~Turbo~~TURBO-PEPSI technique described in ~~the article by~~ S. Posse~~, S.~~ *et al.*, ~~in~~ PROC. ISMRM, p. 299 (1998), ~~page 299. Reference is hereby made to the entire text of this publication~~the disclosure of which is incorporated by reference herein in its entirety.

Following signal excitation, ~~its~~ the method of the present invention records the relaxation behavior ~~is recorded~~ at equidistant time intervals T_E. This is repeated several times at time intervals of T_R seconds. ~~In such an experiment, the~~The signal of each voxel forms a two-dimensional field with the echo times T_E in one direction (DTE) and with the repetitions at the time interval T_R in the other direction (DTR). The relaxation is assumed to be monoexponential, $S = S_0 \exp(-T_E / T_2^*) + g$, with a hardware-dependent noise g that ~~we~~ can be considered ~~as~~ white noise in both domains, DTE and DTR. The values S_0 and T_2^* are constant in DTE but ~~they~~ vary in DTR. The value of S_0 may vary~~,~~ for ~~instance~~example, due to hardware instabilities or blood flow effects, and the value of T_R may vary~~,~~ for ~~instance~~example, due to ~~the~~ test subject stimulation. Variations in T_2^* indicate changes in the local blood flow~~,~~ ~~i~~In the case of relatively small changes ΔS_0 and ΔT_2^*, the signal changes ~~can~~ may be formulated as follows:

$$\frac{\Delta S}{S_0} = \left\{ \left[\left(\frac{T_E}{T_s^*} \right)^2 \left(\frac{\sigma(\Delta T_2^*)}{T_2^*} \right)^2 + \left(\frac{\sigma(\Delta S_0)}{S_0} \right)^2 - 2 \frac{T_E}{T_2^*} \frac{(\Delta S_0 \Delta T_2^*)}{S_0 T_2^*} \right] \varepsilon^{-2T_E/T_2^*} + \left(\frac{\sigma(g)}{S_0} \right)^2 \right\}^{1/2} \quad [1]$$

wherein <A> and σ(A) correspond to the mean value and to the standard deviation of a quantity A in DTR. Further analysis depends on the actual magnitude of the terms used in Equation [1]. ~~It is practical, u~~Under experimental conditions, ~~for~~ ΔS_0 ~~to be~~is negligible ~~both~~ in the resting and ~~in the~~ activation phases (except in the sagital sinus). The quantities $\sigma(\Delta T_2^*)$ and σ(g) ~~are~~ may be determined as follows: (i) adaptation of the signal averaged over the DTR to the monoexponential decay as a function of DTE in order to determine S_0 and T_2^*; (ii) calculation of $\sigma(\Delta T_2^*)$ and σ(g) for each voxel and ~~for~~ each T_E and averaging ~~of~~ these values over the region of interest (ROI); (iii) adaptation of Equation [1] with $\Delta S_0=0$ to these values as a function of T_E. This is possible because local brain activation is ~~manifested~~ shown by an increase of T_2^*, which displays a characteristic T_E-dependence proportional to $T_E e^{-T_R/T_2^*}$, ~~in contrast to which~~whereas the value of the white noise does not depend on T_E (~~see figures~~as shown in the Figures). The T_E-dependence of the signal outside ~~of~~ the brain is approximated by a constant. In order to validate ~~this~~ the method of the present invention, the quantity of white noise is compared to the noise outside ~~of~~ the brain, taking into consideration that ~~u~~ σ(g) is reduced outside ~~of~~ the brain. For a Gaussian distribution, this reduction factor is 0.6028.

Visual stimulation experiments involving four healthy test subjects were ~~carded~~ carried out employing a Siemens Vision-1.5-Tesla scanner. ~~By means of a~~A multi-layer ~~Turbo~~TURBO-PEPSI sequence~~,~~ acquired twelve ~~12~~ EPI images ~~(~~ having a matrix size: of 64 x 32 pixels~~;~~ and a pixel size: of 3 x 6 mm^2~~)~~ ~~were acquired of~~ from a single FID, 90° flip angle at echo times ranging from 12 to 228 ms. A conventional correlation analysis was carried out with the

Stimulate software package, a GUI (Graphical User Interface) based fMRI (functional Magnetic Resonance Imaging) analysis software package, with the use of a boxcar reference vector.

Figure 4 shows ΔS from various voxels averaged over a few ROIs as a function of T_E for two representative persons. The variability of all values over ROIs was small (e.g., 10% to 20%). The ROIs were located in the visual cortex (vc), in the motor cortex (mc), in the white matter (wm), and outside ~~of~~ the brain, circumventing areas outside ~~of~~ the brain that are characterized as phantom images, (out). The filter results from Equation [1] are compiled ~~In~~ in ~~the table;~~ Table 1. ~~wherever~~ Wherever the abbreviated ROI designations are followed by the number of voxels between parentheses, the mean correlation coefficient is normalized over a ~~ROT~~ROI, σ(g) of the ROI outside ~~of~~ the brain, to the mean S_0 of the inner ROIs and the errors in all values are defined as a standard deviation.

Table 1

ROI	ξ	$\sigma(\Delta T_2^*)/T_2$ (%)	$\sigma(g)/S_0$ (%)
vc (20)	0.62 ± 0.21	4.3 ± 0.1	0.75 ± 0.05
mc (20)	-0.11 ± 0.14	0.26 ± 0.16	0.79 ± 0.05
wm (21)	-0.009 ± 0.19	-0.001 ± 5	0.93 ± 0.07
out (21)	-0.19 ± 0.11	not fitted	0.66 ± 0.01
vc (28)	0.67 ± 0.12	3.6 ± 0.1	0.42 ± 0.07
mc (32)	-0.22 ± 0.14	-0.6 ± 0.8	0.72 ± 0.06
wm (32)	-0.29 ± 0.06	-0.4 ± 1.2	0.64 ± 0.06
out (38)	-0.12 ± 0.25	not fitted	0.45 ± 0.01

For all persons, the value of $\sigma(\Delta T_2^*)/T_2^*$ in the activated voxels was significantly increased, ~~in contrast to which~~ whereas there was no significant deviation from ~~0~~ zero in the non-activated voxels. This is why this value has a determining character with a negligible stochastic component.

Consequently, $\sigma(\Delta T_2^*)/T_2^*$ is as suitable as an indicator of regional brain activity as the correlation coefficients of a conventional correlation analysis. In contrast to ~~the~~

~~latter~~conventional correlation analysis, however, $\sigma(\Delta T_2^*)/T_2^*$ displays brain activity for any desired stimulation course, so that it is not necessary to have knowledge of a paradigm. The slight variability of this value over the ROIs ~~would seem to indicate~~indicates that the results for individual voxels are similar to those presented here. This allows the creation of $\sigma(\Delta T_2^*)/T_2^*$ maps. The level of the T_E-independent white noise is very low, ~~which allows the assumption that it~~and thus, stems from the hardware. The S_0 noise is so small that a more precise examination of the S_0 noise is difficult in view of the white noise that is present.

The computer-implemented system and method of the present invention ~~provides for a method for the differentiation~~thus differentiates between an activation, especially ~~a~~ brain activation and noise, whereby no correlation analysis is required. Naturally, the present invention ~~can~~ may also be employed in combination with ~~a~~ other correlation ~~analysis~~ analyses such as, for example, a calculation of correlation coefficients, Z scores, or the application of a t-test, ~~so as to be able~~ to check the results obtained in this manner. However, with the present invention, there is no need for a correlation analysis with two different measurements, one ~~of which takes place~~ with stimulation ~~while~~ and the other ~~takes place~~ without stimulation. For comparison purposes, however, it is possible to include a correlation analysis in which correlation coefficients between the course of time of the stimulator ("reference vector") and the signal changes in pixels of the image are ascertained.

High values for the correlation coefficient ascertained in this process ~~can~~ may be regarded as an activity indicator and reproduced as additional information in slice images or volume images~~, for instance,~~ in the case of a graphic representation of the measured data.

The present invention is particularly well-suited for applications in areas where complicated activations ~~take place~~occur. For this reason, the computer-implemented system and

method ~~according to~~of the present invention ~~and the computer according to the invention~~ are especially suitable for analyzing higher cognitive brain functions, such as emotions, memory, and imagination.

The present invention ~~entails~~ provides numerous advantages over conventional methods and systems, including:~~. These include~~ ~~an~~ optimization of the measuring sensitivity for a quantitative measurement of the relaxation time and of the qualitative relaxation time change;~~. This allows the~~ use of imaging ~~having~~ with the highest possible bandwidth (shortest encoding time) for the smallest spatial distortion possible; and ~~also to achieve~~ maximum measuring sensitivity by measuring an optimal number of encodings following signal excitation.

The ~~analysis~~ system and method of the present invention may ~~can~~ be used in real time measurements in order to directly analyze the relaxation changes.

In addition, the ~~analysis methods according to~~system and method of the present invention are particularly versatile. It has been proven to be practical to employ a summation or, even more advantageously, a weighted summation which, in comparison to a curve adaptation, can be done faster and without any loss of the measuring sensitivity. A summation, or a weighted summation, ~~has the advantage that~~are advantageous because they ~~it constitutes~~constitute ~~a~~ particularly reliable analysis methods.

All of the test subjects exhibited a strong activation in the primary visual cortex (V_1) and in the neighboring regions. The changes observed in the functional signal measured with TURBO-PEPSI amount to up to 10%, depending on the relaxation time T_2^*, the position, and the test subject in question.

The excitation ~~exhibits~~ exhibited a maximum in the vicinity of $T_E = T_2^*$. A comparison of EPI and TURBO-PEPSI images with $T_E = 72.5$ ms revealed very similar activation images.

The gain in sensitivity is particularly advantageous for real time measurements since a change in the relaxation ~~can~~ may be effectively ascertained, even with just a few measured values. In summary, ~~it can be said that~~ the multi-echo detection of the differential signal of the present invention provides ~~translates into~~ optimal sensitivity for various magnetic field strengths.

Furthermore, the invention can be utilized in echo-planar imaging (EPI), ~~in~~ phase-encoded imaging methods, as well as ~~in~~ spectroscopic imaging methods.

It will be apparent to those skilled in the art that various modifications and variations can be made in the computer-implemented system and method of the present invention and in construction of the system and method without departing from the scope or spirit of the invention. As an example, ~~The examples presented serve to elucidate the computer arid the analysis method on the basis of NMR measurements on the human brain. Naturally, the computer, the nuclear resonance tomograph as well as the analysis method can~~the computer-implemented system and method of the present invention may also be used to examine other samples of either living or non-living material, other than the human brain.~~.~~

Other embodiments of the invention will be apparent to those skilled in the art from consideration of the specification and practice of the invention disclosed herein. It is intended that the specification and examples be considered as exemplary only, with a true scope and spirit of the invention being indicated by the following claims.